

# Package ‘FBCanalysis’

March 22, 2022

**Title** Develop and evaluate time series data models based on fluctuation based clustering

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**Description** The package includes tools for performing fluctuation-based clustering (FBC) on biological time series data, primarily for monitoring data fluctuations in asthmatics. The package includes functions for registering and processing time series data, developing matching clustering models based on Earth Mover's distances, and evaluating the models through enrichment analysis, stability after random data removal, or other frequently used cluster stability metrics.

**License** MIT + file LICENSE

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**URL** <https://github.com/MrMaximumMax/FBCanalysis>

**BugReports** <https://github.com/MrMaximumMax/FBCanalysis/issues>

**Depends** R (>= 4.1.1)

**Imports** arsenal,  
cluster,  
clValid,  
dplyr,  
emdist,  
FCPS,  
glmnet,  
imputeTS,  
lubridate,  
mclust,  
RankAggreg,  
readr,  
stats,  
utils

**Suggests** rmarkdown,  
knitr

**VignetteBuilder** knitr

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add_clust2enrich	<i>Add clustering assignments to enrichment data frame</i>
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---

### Description

Add clustering assignments to enrichment data frame

### Usage

```
add_clust2enrich(enrich, clustdat)
```

### Arguments

enrich	Preprocessed enrichment data frame (also see function: <a href="#">add_enrich</a> )
clustdat	Object of type list storing clustering data (also see function: <a href="#">clust_matrix</a> )

### Value

Processed enrichment data frame with added column indicating cluster assignments

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
clustering <- clust_matrix(matrix, method = "kmeans", nclust = 3)
enr <- add_enrich(list, '../enrichment_dat.csv') #file can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/enrichment)
enr <- add_clust2enrich(enr, clustering)
```

---

add\_clust2ts

---

*Add clustering assignments to time series data*


---

**Description**

Add clustering assignments to time series data

**Usage**

```
add_clust2ts(plist, clustdat)
```

**Arguments**

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
clustdat	Object of type list storing clustering data (also see function: <a href="#">clust_matrix</a> )

**Value**

Processed data frame storing time series data with added column indicating cluster assignments

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
clustering <- clust_matrix(matrix, method = "kmeans", nclust = 3)
ts <- add_clust2ts(list, clustering)
```

---

add\_enrich

---

*Add enrichment data and preprocess for analysis*


---

**Description**

Add enrichment data and preprocess for analysis

**Usage**

```
add_enrich(plist, path)
```

**Arguments**

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
path	Path where enrichment csv file is stored

**Value**

Processed data as object of type data frame; Enrichment data Patient\_IDs are matched with Time Series Data List Patient IDs; In case it was indicated, NA values in the enrichment data are filled up by random sampling

**Examples**

```
list <- patient_list('.../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
enr <- add_enrich(list, '.../enrichment_dat.csv') #file can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/enrichment)
```

---

clust_matrix	<i>Cluster Earth Mover Distance Square Matrix data</i>
--------------	--

---

**Description**

Cluster Earth Mover Distance Square Matrix data

**Usage**

```
clust_matrix(matrix, method, nclust, plotclust)
```

**Arguments**

matrix	Object of type matrix storing Earth Mover's Distances for patient time series data distribution pairs
method	Clustering method (hierarchical, kmeans, diana, fanny, som, modelbased, sota, pam, clara)
nclust	Number of clusters (if not specified, user will be asked in the terminal)
plotclust	TRUE/FALSE if clustering data should be visualized (TRUE by default)

**Value**

Object of type list storing cluster data and clustering assignments for the Patient\_IDs from the Earth Mover's Distance matrix

**Examples**

```
list <- patient_list('.../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
matrix <- emd_matrix(list, "FEV1")
clustering <- clust_matrix(matrix, method = "hierarchical", nclust = 2)
```

---

clValid_flow	<i>Interactive console workflow to calculate and evaluate cluster validation measures</i>
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---

**Description**

Interactive console workflow to calculate and evaluate cluster validation measures

**Usage**

```
clValid_flow(matrix, par)
```

**Arguments**

matrix	Earth Mover's Distance Matrix for processed patient time series data (also see functions: <a href="#">emd_matrix</a> , <a href="#">patient_list</a> )
par	Object of type list storing clustering methods and cluster range of interest; initialized via function: <a href="#">init_clValid</a>

**Value**

Object of type list storing chosen clustering method and number of clusters (can be then used for function [clust\\_matrix](#))

**Examples**

```
list <- patient_list('../ts_demofiles2') #file can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles2)
#Sampling frequency is twice daily
distmat <- emd_matrix(list, "PEF", maxIter = 5000)
parameters <- init_clValid()
output <- clValid_flow(distmat, parameters)
clustdat <- clust_matrix(distmat, output$method, as.numeric(output$clust_num))
```

---

emd_heatmap	<i>Visualize an Earth Mover's Distance Square Matrix as a heatmap</i>
-------------	---

---

**Description**

Visualize an Earth Mover's Distance Square Matrix as a heatmap

**Usage**

```
emd_heatmap(input, parameter)
```

**Arguments**

input	Earth Mover's Distance Matrix or list storing patient time series data (also see function: <a href="#">patient_list</a> )
parameter	In case list is input, the parameter of interest from time series data list

**Value**

Visualized Earth Mover's Distance Matrix as a heatmap

**Examples**

```
list <- patient_list('.../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
matrix <- emd_matrix(list, "FEV1")
emd_heatmap(matrix)
```

---

emd_matrix	<i>Generate a Earth Mover's Distance Matrix out of time series data list entries</i>
------------	--

---

**Description**

Generate a Earth Mover's Distance Matrix out of time series data list entries

**Usage**

```
emd_matrix(plist, parameter, maxIter)
```

**Arguments**

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest to determine Earth Mover's Distances between distributions
maxIter	Maximum of iterations to calculate Earth Mover's Distance (default: 500)

**Value**

Earth Mover's Distance Square Matrix of type matrix

**Examples**

```
list <- patient_list('.../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
matrix <- emd_matrix(list, "FEV1")
```

---

enr_obs_clust	<i>Observe specific cluster for overview and p-values</i>
---------------	---

---

**Description**

Observe specific cluster for overview and p-values

**Usage**

```
enr_obs_clust(ts.dat, enrich, clustno)
```

**Arguments**

ts.dat	Processed data frame storing time series data and cluster assignments (also see function: <a href="#">add_clust2ts</a> )
enrich	Processed data frame storing enrichment data and cluster assignments (also see function: <a href="#">add_clust2enrich</a> )
clustno	Cluster number of interest

**Value**

Terminal output presenting summary of time series and enrichment data with corresponding p-values

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
clustering <- clust_matrix(matrix, method = "kmeans", nclust = 3)
enr <- add_enrich(list, '../enrichment_dat.csv') #file can be drawn from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/enrichment)
enr <- add_clust2enrich(enr, clustering)
ts <- add_clust2ts(list, clustering)
enr_obs_clust(ts, enr, 1)
```

---

init_clValid	<i>Initialize Cluster Validation Measure Analysis in the context of Fluctuation Based Clustering (FBC) analysis</i>
--------------	---

---

**Description**

Initialize Cluster Validation Measure Analysis in the context of Fluctuation Based Clustering (FBC) analysis

**Usage**

```
init_clValid()
```

**Value**

Object of type list storing cluster method(s) and number of cluster range of interest (to be used for function: [clValid\\_flow](#))

**Examples**

```
init_clValid()
```

---

jaccard_run_cognate	<i>Simulate random data removal from time series data list and determine Jaccard index via Cognate Cluster approach for multiple random data removal steps</i>
---------------------	--

---

**Description**

Simulate random data removal from time series data list and determine Jaccard index via Cognate Cluster approach for multiple random data removal steps

**Usage**

```
jaccard_run_cognate(
  plist,
  parameter,
  n_simu,
  method,
  clust_num,
  n_clust,
  range
)
```

**Arguments**

plist	Object of type list storing patient time series data (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest in time series data list
n_simu	Number of simulations
method	Clustering method (also see function: <a href="#">clust_matrix</a> )
clust_num	Cluster of interest
n_clust	Number of clusters
range	Range to simulate random data removal (e.g. c(0.1,0.2,0.5,0.7,0.8))

**Value**

Object of type list storing Jaccard indices for each indicated random data removal step and visualized results in a boxplot



## Examples

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
output <- jaccard_run_cognate(list,"PEF",10,"hierarchical",1,3,c(0.005,0.01,0.05,0.1,0.2))
```

---

jaccard_run_emd	<i>Simulate random data removal from time series data list and determine Jaccard index via Earth Mover's Distance approach for multiple random data removal steps</i>
-----------------	---

---

## Description

Simulate random data removal from time series data list and determine Jaccard index via Earth Mover's Distance approach for multiple random data removal steps

## Usage

```
jaccard_run_emd(plist, parameter, n_simu, method, clust_num, n_clust, range)
```

## Arguments

plist	Object of type list storing patient time series data (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest in time series data list
n_simu	Number of simulations
method	Clustering method (also see function: <a href="#">clust_matrix</a> )
clust_num	Cluster of interest
n_clust	Number of clusters
range	Range to simulate random data removal (e.g. c(0.1,0.2,0.5,0.7,0.8))

## Value

Object of type list storing Jaccard indices for each indicated random data removal step and visualized results in a boxplot

## Examples

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
output <- jaccard_run_emd(list,"PEF",10,"hierarchical",1,3,c(0.005,0.01,0.05,0.1,0.2))
```

---

max_fluc	<i>Determine pair of maximum fluctuation difference in a list storing time series data</i>
----------	--

---

### Description

Determine pair of maximum fluctuation difference in a list storing time series data

### Usage

```
max_fluc(plist, parameter)
```

### Arguments

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest from time series data list

### Value

Console output with Patient\_ID pair, corresponding Earth Mover's Distance and visualized boxplot of both time series data distributions

### Examples

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
matrix <- emd_matrix(list, "FEV1")
max_fluc(list, "PEF")
```

---

patient_boxplot	<i>Visualize patient(s) time series data in a boxplot for indicated parameter</i>
-----------------	---

---

### Description

Visualize patient(s) time series data in a boxplot for indicated parameter

### Usage

```
patient_boxplot(plist, patients, parameter, normalized)
```

### Arguments

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
patients	Patient_ID(s) referring to (a) list element; can be single ID or multiple IDs (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest in list element(s)
normalized	TRUE/FALSE if z-normalized (TRUE by default)

**Value**

Visualized patient(s) time series data in a boxplot for indicated parameter

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
patient_boxplot(list,c("ID_2","testpat_1","testpat_2","a301"), "FEV1")
```

---

patient_hist	<i>Visualize patient time series data in a histogram for indicated parameter</i>
--------------	--

---

**Description**

Visualize patient time series data in a histogram for indicated parameter

**Usage**

```
patient_hist(plist, Patient_ID, parameter, normalized)
```

**Arguments**

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
Patient_ID	Patient_ID referring to a list element (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest in list element
normalized	TRUE/FALSE if z-normalized (TRUE by default)

**Value**

Visualized patient time series data in a histogram for indicated parameter

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
patient_hist(list,"testpat_1","PEF")
```

---

patient_list	<i>Process patient time series data by interpolation options and store data in an object of type list</i>
--------------	---

---

**Description**

Process patient time series data by interpolation options and store data in an object of type list

**Usage**

```
patient_list(path)
```

**Arguments**

path	Path where csv file(s) are stored (only folder, not specific file(s))
------	---

**Value**

Object of type list storing patient time series data

**Examples**

```
list <- patient_list('../ts_demofiles1') #files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
```

---

patient_ts_plot	<i>Visualize patient time series data in a time series plot for indicated parameter</i>
-----------------	---

---

**Description**

Visualize patient time series data in a time series plot for indicated parameter

**Usage**

```
patient_ts_plot(plist, Patient_ID, parameter, normalized)
```

**Arguments**

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
Patient_ID	Patient_ID referring to a list element (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest in list element
normalized	TRUE/FALSE if z-normalized (TRUE by default)

**Value**

Visualized patient time series data in a time series plot for indicated parameter

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
patient_ts_plot(list,"testpat_1","PEF")
```

---

rnd_dat_rm	<i>Remove random data from time series data list</i>
------------	--

---

**Description**

Remove random data from time series data list

**Usage**

```
rnd_dat_rm(plist, removal)
```

**Arguments**

plist	Object of type list storing patient time series data (also see function: <a href="#">patient_list</a> )
removal	Amount of data removal (0 = 0%, 1 = 100%)

**Value**

Object of type list storing patient time series data with indicated amount of data removed randomly

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
list_rm <- rnd_dat_rm(testlist, 0.95)
```

---

sim_jaccard_cognate	<i>Simulate random data removal from time series data list and determine Jaccard index via Cognate Cluster approach</i>
---------------------	---

---

**Description**

Simulate random data removal from time series data list and determine Jaccard index via Cognate Cluster approach

**Usage**

```
sim_jaccard_cognate(plist, parameter, removal, n_simu, method, n_clust, Iter)
```

**Arguments**

plist	Object of type list storing patient time series data (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest in time series data list
removal	Amount of random data removal to determine Jaccard index
n_simu	Number of simulations
method	Clustering method (also see function: <a href="#">clust_matrix</a> )
n_clust	Number of clusters (also see function: <a href="#">clust_matrix</a> )
Iter	Maximum iterations to determine Earth Mover's Distances (also see function: <a href="#">emd_matrix</a> ); default is 5,000 for this function

**Value**

Object of type matrix storing received Jaccard indices for indicated amount of random data removal for all clusters

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
output <- sim_jaccard_cognate(list, "PEF", 0.05, 10, "hierarchical", 2, 1000)
```

---

sim_jaccard_emd	<i>Simulate random data removal from time series data list and determine Jaccard index via Earth Mover's Distance approach</i>
-----------------	--

---

**Description**

Simulate random data removal from time series data list and determine Jaccard index via Earth Mover's Distance approach

**Usage**

```
sim_jaccard_emd(plist, parameter, removal, n_simu, method, n_clust, Iter)
```

**Arguments**

plist	Object of type list storing patient time series data (also see function: <a href="#">patient_list</a> )
parameter	Parameter of interest in time series data list
removal	Amount of random data removal to determine Jaccard index
n_simu	Number of simulations
method	Clustering method (also see function: <a href="#">clust_matrix</a> )
n_clust	Number of clusters (also see function: <a href="#">clust_matrix</a> )
Iter	Maximum iterations to determine Earth Mover's Distances (also see function: <a href="#">emd_matrix</a> ); default is 5,000 for this function

**Value**

Object of type matrix storing received Jaccard indices for indicated amount of random data removal for all clusters

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
output <- sim_jaccard_emd(list, "PEF", 0.05, 10, "hierarchical", 2, 1000)
```

---

sim_sample_enr	<i>Simulate random sampling for NA entries in enrichment data and check stability of resulting p-values for the enrichment parameters</i>
----------------	---

---

**Description**

Simulate random sampling for NA entries in enrichment data and check stability of resulting p-values for the enrichment parameters

**Usage**

```
sim_sample_enr(plist, path, clustdat, clustno, n_sim)
```

**Arguments**

plist	List storing patient time series data (also see function: <a href="#">patient_list</a> )
path	Path where enrichment csv file is stored
clustdat	Object of type list storing clustering data (also see function: <a href="#">clust_matrix</a> )
clustno	Cluster number of interest
n_sim	Number of simulations

**Value**

Object of type list storing the received p-values for each parameter in a vector and boxplot visualizing the received p-values

**Examples**

```
list <- patient_list('../ts_demofiles1') #Just folder; files can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/ts_demofiles1)
#Sampling frequency is supposed to be daily
path <- '../enrichment.csv' #Enrichment file can be pulled from GitHub demo files
#(https://github.com/MrMaximumMax/FBCanalysis/tree/master/demo_and_testfiles/enrichment)
test <- sim_sample_enr(list,path,clustering,1,100)
sim_sample_enr <- function(plist, path, clustdat, clustno, n_sim)
```

---

`znorm`*z-normalise data*

---

**Description**

Function applicable on any numeric distribution of data and z-normalize them.

**Usage**

```
znorm(data)
```

**Arguments**

<code>data</code>	Numeric distribution; may be stored in an object of type vector, matrix or data frame
-------------------	---

**Value**

z-normalized distribution of input

**Examples**

```
random_distribution <- runif(n = 50, min = 1, max = 10)
znorm_distribution <- znorm(random_distribution)
```



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